Notice of Allowability	Application No.	Applicant(s)	
	10/519,106	NAKADE ET AL.	
	Examiner	Art Unit	
	Christina Marchetti Bradley	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to *the amendmen filed 4/17/2007*.

2. ☒ The allowed claim(s) is/are *7,9,11 and 15-17*.

3. ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
   a) ☒ All b) ☐ Some* c) ☐ None of the:
      1. ☒ Certified copies of the priority documents have been received.
      2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
      3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

   * Certified copies not received: _____.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.
THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

4. ☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.

5. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
   (a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review (PTO-948) attached
      1) ☐ hereto or 2) ☐ to Paper No./Mail Date _____.
   (b) ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date _____.

   Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).

6. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

1. ☐ Notice of References Cited (PTO-892)
2. ☐ Notice of Draftperson's Patent Drawing Review (PTO-948)
3. ☐ Information Disclosure Statements (PTO/SB/08), Paper No./Mail Date _____
4. ☐ Examiner's Comment Regarding Requirement for Deposit of Biological Material
5. ☐ Notice of Informal Patent Application
6. ☐ Interview Summary (PTO-413), Paper No./Mail Date _____ .
7. ☒ Examiner's Amendment/Comment
8. ☐ Examiner's Statement of Reasons for Allowance
9. ☐ Other _____.

EXAMINER'S AMENDMENT

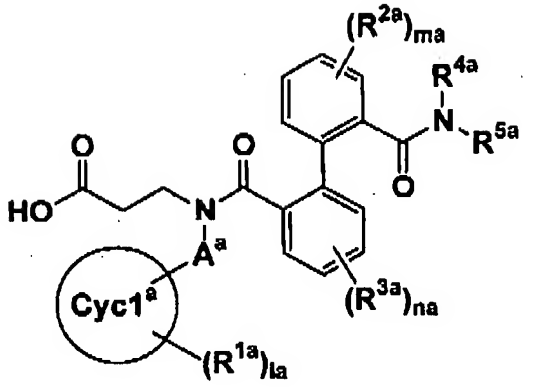
An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

Authorization for the examiner's amendment was given by Susan Mack on 5/22/2007.

1. - 6. (canceled)

7. **(currently amended):** A method for the treatment of a chronic disease selected from the group consisting of chronic asthma, glomerular nephritis, obesity, prostate hyperplasia, a disease induced by the progress of arteriosclerosis, and rheumatoid or atopic dermatitis, wherein said method comprises administering to a mammal having said chronic disease an effective amount of an EDG-2 antagonist,

wherein the EDG-2 antagonist is a β-alanine derivative of formula (I)



(I)

wherein A^a is, (1) C1-6 alkylene, (2) C2-6 alkenylene, or (3) C2-6 alkynylene, wherein A^a may be substituted with 1-3 of C1-4 alkyl,

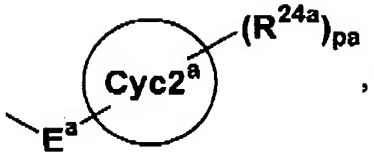
$Cyc1^a$ is, (1) C3-15 carboring, or (2) 3-15 membered heteroring having 1-4 of nitrogen, 1-2 of oxygen and/or 1-2 of sulfur,

R^{1a} is (1) C1-4 alkyl, (2) halogen, (3) cyano, (4) trihalomethyl, (5) $-OR^{6a}$, (6) $-SR^{7a}$, (7) $-NR^{8a}R^{9a}$, (8) nitro, (9) $-COOR^{10a}$, (10) $-CONR^{11a}R^{12a}$, (11) $-NR^{13a}COR^{14a}$, (12) $-SO_2NR^{15a}R^{16a}$, (13) $-NR^{17a}SO_2R^{18a}$, (14) $-S(O)R^{19a}$, or (15) $-SO_2R^{20a}$,

R^{6a}, R^{7a}, R^{8a}, R^{9a}, R^{10a}, R^{11a}, R^{12a}, R^{13a}, R^{14a}, R^{15a}, R^{16a}, R^{17a}, R^{18a}, R^{19a} and R^{20a} are each independently, (1) hydrogen, or (2) C1-4 alkyl,

R^{2a} and R^{3a} are each independently, (1) C1-4 alkyl, (2) C1-4 alkoxy, or (3) halogen,

R^{4a} and R^{5a} are each independently, (1) hydrogen, (2) C1-4 alkyl, (3) C2-4 alkenyl, (4) C2-4 alkynyl, (5) C1-4 alkyl substituted with $-OR^{21a}$, (6) C1-4 alkyl substituted with $-NR^{22a}R^{23a}$ or

(7) 

, or

R^{4a} and R^{5a} are taken together with the nitrogen to which they are attached to form a 3-15 membered mono-, bi- or tri-cyclic heteroring, wherein the heteroring represents at least one nitrogen and it may be substituted with C1-4 alkyl substituted with $-OR^{25a}$,

R^{21a}, R^{22a}, R^{23a} and R^{25a} are each independently, (1) hydrogen, (2) C1-4 alkyl, (3) C2-6 acyl, or (4) trihaloacetyl,

E^a is (1) a bond, (2) C1-6 alkylene, (3) C2-6 alkenylene, or (4) C2-6 alkynylene, wherein E^a may be substituted with 1-3 of (1) C1-4alkyl, or (2) C1-4 alkyl substituted with $-OR^{26a}$,

R^{26a} is (1) hydrogen, (2) C1-4 alkyl, (3) C2-6 acyl, or (4) trihaloacetyl, $Cyc2^a$ is (1) C3-15 carboring, or (2) 3-15 membered heteroring having 1-4 of nitrogen, 1-2 of oxygen and/or 1-2 of sulfur,

R^{24a} is (1) C1-4 alkyl, (2) halogen, (3) cyano, (4) trihalomethyl, (5) $-OR^{27a}$, (6) $-SR^{28a}$, (7) $-NR^{29a}R^{30a}$, (8) nitro, (9) $-COOR^{31a}$, (10) $-CONR^{32a}R^{33a}$, (11) $-NR^{34a}COR^{35a}$, (12) $-SO_2NR^{36a}R^{37a}$, (13) $-NR^{38a}SO_2R^{39a}$, (14) $-S(O)R^{40a}$, or (15) $-SO_2R^{41a}$,

R^{27a}, R^{28a}, R^{29a}, R^{30a}, R^{31a}, R^{32a}, R^{33a}, R^{34a}, R^{35a}, R^{36a}, R^{37a}, R^{38a}, R^{39a}, R^{40a} and R^{41a} are each independently (1) hydrogen, or (2) C1-4 alkyl,

ia is 0 or an integer of 1 to 5, ma is 0 or an integer of 1 to 4, and

na is 0 or an integer of 1 to 4, pa is 0 or an integer of 1 to 5, and

wherein when ia is 2 or more, R^{1a}'s are the same or different,

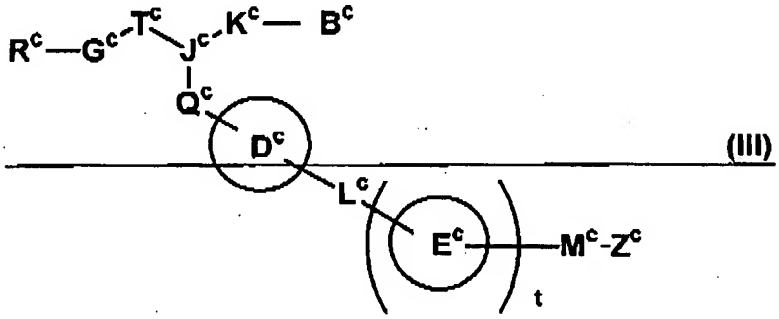
when ma is 2 or more, R^{2a}'s are the same or different,

when na is 2 or more, R^{3a}'s are the same or different, and

when pa is 2 or more, they are the same or different, or

a prodrug thereof or a salt thereof;

~~or the EDG 2 antagonist is a compound of formula (III)~~



~~wherein R^e is optionally substituted aliphatic hydrocarbon or a ring group optionally having substituent(s),~~

~~G^e is a bond or a spacer having a main chain of 1 to 8 atoms,~~

~~T^e is $-CH_2-$ or a spacer having a main chain of 1 atom having a hydrogen bond accepting group optionally having substituent(s),~~

~~J^e is nitrogen or carbon,~~

~~B^e is optionally substituted aliphatic hydrocarbon or a ring group optionally having substituent(s),~~

~~K^e is (1) a bond or (2) a spacer having a main chain of 1 to 8 atoms which may form a ring together with the substituent of the ring group represented by R^e, ring D^e or the substituent of the ring D^c;~~

~~Q^c is (1) a bond or (2) a spacer having a main chain of 1 to 8 atoms which may form a ring together with the ring group represented by R^c, a substituent of the ring group represented by R^e, or K^e;~~

~~ring D^e is a ring optionally having more substituent(s);~~

~~L^e is a bond or a spacer having a main chain of 1 to 3 atoms;~~

~~ring E^e is, a ring group optionally having substituent(s);~~

~~M^e is a bond or a spacer having a main chain of 1 to 8 atoms;~~

~~Z^e is an acidic group, and~~

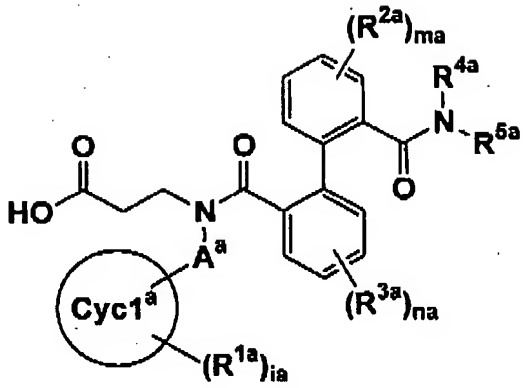
~~t is 0 or 1, or~~

~~a salt thereof.~~

8. (canceled).

9. (currently amended) A pharmaceutical composition comprising an EDG-2 antagonist in combination with one or more selected from LPA receptor antagonist, anti-androgenergic agent, α1 receptor blocker or 5α-reductase inhibitor,

wherein the EDG-2 antagonist is a β-alanine derivative of formula (I)



(I)

wherein A^a is, (1) C1-6 alkylene, (2) C2-6 alkenylene, or (3) C2-6 alkynylene, wherein A^a may be substituted with 1-3 of C1-4 alkyl,

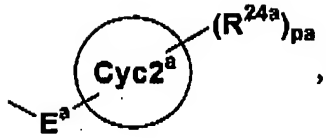
$Cyc1^a$ is, (1) C3-15 carboring, or (2) 3-15 membered heteroring having 1-4 of nitrogen, 1-2 of oxygen and/or 1-2 of sulfur,

R^{1a} is (1) C1-4 alkyl, (2) halogen, (3) cyano, (4) trihalomethyl, (5) $-OR^{6a}$, (6) $-SR^{7a}$, (7) $-NR^{8a}R^{9a}$, (8) nitro, (9) $-COOR^{10a}$, (10) $-CONR^{11a}R^{12a}$, (11) $-NR^{13a}COR^{14a}$, (12) $-SO_2NR^{15a}R^{16a}$, (13) $-NR^{17a}SO_2R^{18a}$, (14) $-S(O)R^{19a}$, or (15) $-SO_2R^{20a}$,

R^{6a}, R^{7a}, R^{8a}, R^{9a}, R^{10a}, R^{11a}, R^{12a}, R^{13a}, R^{14a}, R^{15a}, R^{16a}, R^{17a}, R^{18a}, R^{19a} and R^{20a} are each independently, (1) hydrogen, or (2) C1-4 alkyl,

R^{2a} and R^{3a} are each independently, (1) C1-4 alkyl, (2) C1-4 alkoxy, or (3) halogen,

R^{4a} and R^{5a} are each independently, (1) hydrogen, (2) C1-4 alkyl, (3) C2-4 alkenyl, (4) C2-4 alkynyl, (5) C1-4 alkyl substituted with $-OR^{21a}$, (6) C1-4 alkyl substituted with $-NR^{22a}R^{23a}$ or

(7)  , or

R^{4a} and R^{5a} are taken together with the nitrogen to which they are attached to form a 3-15 membered mono-, bi- or tri-cyclic heteroring, wherein the heteroring represents at least one nitrogen and it may be substituted with C1-4 alkyl substituted with $-OR^{25a}$,

R^{21a}, R^{22a}, R^{23a} and R^{25a} are each independently, (1) hydrogen, (2) C1-4 alkyl, (3) C2-6 acyl, or (4) trihaloacetyl,

E^a is (1) a bond, (2) C1-6 alkylene, (3) C2-6 alkenylene, or (4) C2-6 alkynylene, wherein E^a may be substituted with 1-3 of (1) C1-4alkyl, or (2) C1-4 alkyl substituted with $-OR^{26a}$,

R^{26a} is (1) hydrogen, (2) C1-4 alkyl, (3) C2-6 acyl, or (4) trihaloacetyl, $Cyc2^a$ is (1) C3-15 carboring, or (2) 3-15 membered heteroring having 1-4 of nitrogen, 1-2 of oxygen and/or 1-2 of sulfur,

R^{24a} is (1) C1-4 alkyl, (2) halogen, (3) cyano, (4) trihalomethyl, (5) $-OR^{27a}$, (6) $-SR^{28a}$, (7) $-NR^{29a}R^{30a}$, (8) nitro, (9) $-COOR^{31a}$, (10) $-CONR^{32a}R^{33a}$, (11) $-NR^{34a}COR^{35a}$, (12) $-SO_2NR^{36a}R^{37a}$, (13) $-NR^{38a}SO_2R^{39a}$, (14) $-S(O)R^{40a}$, or (15) $-SO_2R^{41a}$,

R^{27a}, R^{28a}, R^{29a}, R^{30a}, R^{31a}, R^{32a}, R^{33a}, R^{34a}, R^{35a}, R^{36a}, R^{37a}, R^{38a}, R^{39a}, R^{40a} and R^{41a} are each independently (1) hydrogen, or (2) C1-4 alkyl,

ia is 0 or an integer of 1 to 5, ma is 0 or an integer of 1 to 4, and

na is 0 or an integer of 1 to 4, pa is 0 or an integer of 1 to 5, and

wherein when ia is 2 or more, R^{1a}'s are the same or different,

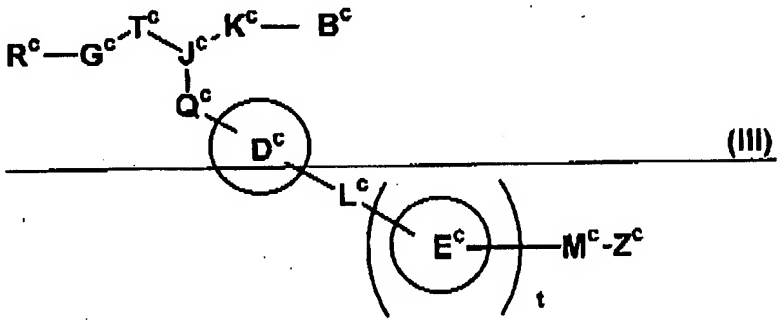
when ma is 2 or more, R^{2a}'s are the same or different,

when na is 2 or more, R^{3a}'s are the same or different, and

when pa is 2 or more, they are the same or different, or

a prodrug thereof or a salt thereof;

~~or the EDG-2 antagonist is a compound of formula (III)~~



(III)

~~wherein R^c is optionally substituted aliphatic hydrocarbon or a ring group optionally having substituent(s),~~

~~G^c is a bond,~~

~~T^c is $-CH_2-$ or a spacer having a main chain of 1 atom having a hydrogen bond accepting group optionally having substituent(s),~~

~~J^c is nitrogen or carbon,~~

~~B^c is optionally substituted aliphatic hydrocarbon or a ring group optionally having substituent(s),~~

~~K^e is (1) a bond or (2) a spacer having a main chain of 1 to 8 atoms which may form a ring together with the substituent of the ring group represented by R^e, ring D^e or the substituent of the ring D^e;~~

~~Q^e is (1) a bond or (2) a spacer having a main chain of 1 to 8 atoms which may form a ring together with the ring group represented by R^e, a substituent of the ring group represented by R^e, or K^e;~~

~~ring D^e is a ring optionally having more substituent(s);~~

~~L^e is a bond or a spacer having a main chain of 1 to 3 atoms;~~

~~ring E^e is selected from the group consisting of benzene optionally having substituent(s), piperidine optionally having substituent(s), isoxazole optionally having substituent(s), pyrazole optionally having substituent(s), pyridine optionally having substituent(s), thiazole optionally having substituent(s), imidazole optionally having substituent(s), pyrrole optionally having substituent(s), and pyrrolidine optionally having substituent(s);~~

~~M^e is a bond or a spacer having a main chain of 1 to 8 atoms;~~

~~Z^e is an acidic group, and~~

~~t is 0 or 1, or~~

~~a salt thereof.~~

10. (canceled).

11. (previously presented): The method according to claim 7, wherein the chronic disease is prostate hyperplasia.

12.-14. (canceled).

15. (previously presented): The method according to claim 7, wherein the method comprises administering to said mammal one or more members selected from the group consisting of an LPA receptor antagonist, an anti-androgenergic agent, an $\alpha 1$ receptor blocker, and an 5α-reductase inhibitor, in combination with the EDG-2 antagonist.

16. (previously presented): The pharmaceutical composition according to claim 9, wherein the pharmaceutical composition is effective for treatment of a chronic disease selected from the group consisting of chronic asthma, glomerular nephritis, obesity, prostate hyperplasia, a disease induced by the progress of arteriosclerosis, and rheumatoid or atopic dermatitis.

17. (currently amended): The pharmaceutical composition according to claim 16, wherein the composition is effective for the treatment of prostate hyperplasia.

18.-21. (canceled).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christina Marchetti Bradley whose telephone number is (571) 272-9044. The examiner can normally be reached on Monday through Friday, 8:30 A.M. to 5:00 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on (571) 272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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Patent Examiner
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